



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 39/395, C12N 15/11, A61K 38/17, C12N 15/63, G01N 33/68, C07K 14/47, A01K 67/027, A61P 37/00	A3	(11) International Publication Number: WO 00/21559 (43) International Publication Date: 20 April 2000 (20.04.00)
(21) International Application Number: PCT/US99/23485 (22) International Filing Date: 8 October 1999 (08.10.99) (30) Priority Data: 60/103,660 9 October 1998 (09.10.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/103,660 (CIP) Filed on 9 October 1998 (09.10.98) (71) Applicant (for all designated States except US): MUSC FOUNDATION FOR RESEARCH DEVELOPMENT [US/US]; Suite 305, Cannon Park Place, 141 MUSC Complex, Charleston, SC 29425 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): GILKESON, Gary [US/US]; 843 Whispering Marsh Drive, Charleston, SC 29412 (US). WATANABE, Hiroshi [JP/US]; Apartment 6E, 1850 Ashley Crossing Lane, Charleston, SC 29414 (US).		(74) Agents: SPRATT, Gwendolyn, D. et al.; Needle & Rosenberg, P.C., Suite 1200, The Candler Building, 127 Peachtree Street, N.E.; Atlanta, GA 30303-1811 (US). (81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> (88) Date of publication of the international search report: 28 September 2000 (28.09.00)
(54) Title: BLOCKING FACTOR B TO TREAT COMPLEMENT-MEDIATED IMMUNE DISEASE (57) Abstract <p>The present invention provides a method of treating or preventing complement-mediated immune disease in a subject, comprising administering to the subject an inhibitor of synthesis or activity of Factor B, whereby the inhibition of synthesis or activity of Factor B treats or prevents the immune disease. Also provided are an antibody to Factor B, an anti-sense oligonucleotide which blocks the mRNA which encodes Factor B and a peptide which competitively binds C3, the receptor for Factor B. The present invention further provides a vector comprising the nucleic acid of this invention and a cell comprising the vector. Also provided is a method of administering to a subject in a pharmaceutically acceptable carrier an antibody, oligonucleotide, peptide and vector of the invention. The present invention further provides a method of determining the predisposition of a subject to complement-mediated immune disease and a method of determining efficacy of treatment in and prognosis of a subject with complement-mediated immune disease. Further, the present invention also provides a mutant transgenic mouse.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China	KZ	Republic of Korea	PT	Portugal		
CU	Cuba	LC	Kazakstan	RO	Romania		
CZ	Czech Republic	LI	Saint Lucia	RU	Russian Federation		
DE	Germany	LK	Liechtenstein	SD	Sudan		
DK	Denmark	LR	Sri Lanka	SE	Sweden		
EE	Estonia		Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 99/23485

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/395 C12N15/11 A61K38/17 C12N15/63 G01N33/68
C07K14/47 A01K67/027 A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EMBASE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	C. CLARDY ET AL.: "In vitro inhibition of complement activation using a monoclonal antibody (MoAb) directed against human factor B (Fb)." PEDIATRIC RESEARCH, vol. 31, no. 4 part 2, 1992, page 331A XP000907515 Basel, Switzerland abstract 1969 ----- -/--	1-8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search 20 June 2000	Date of mailing of the international search report 28/06/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Nooij, F

INTERNATIONAL SEARCH REPORT

Int lional Application No
PCT/US 99/23485

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	S. MIYAGAWA ET AL.: "Prolonging discordant xenograft survival with anticomplement reagents K76COOH and FUT175." TRANSPLANTATION, vol. 55, no. 4, April 1993 (1993-04), pages 709-713, XP000907527 Baltimore, MD, USA abstract page 711, right-hand column, line 11 - line 34	1-3
A	J. SUNDSMO ET AL.: "Factor B, the complement alternative pathway serine proteinase, is a major constitutive protein synthesized and secreted by resident and elicited mouse macrophages." THE JOURNAL OF EXPERIMENTAL MEDICINE, vol. 161, no. 2, 1 February 1985 (1985-02-01), pages 306-322, XP000907493 New York, NY, USA the whole document	1-20
A	K. TRAUSTADOTTIR ET AL.: "Participation of factor B in residual immune complex red cell binding activity observed in serum from a C2-deficient systemic lupus erythematosus patient may delay the appearance of clinical symptoms." ARTHRITIS & RHEUMATISM, vol. 41, no. 3, March 1998 (1998-03), pages 427-434, XP000907526 New York, NY, USA abstract discussion	1-8,16, 17,20
A	M. FRANK: "Animal models for complement deficiencies." JOURNAL OF CLINICAL IMMUNOLOGY, vol. 15, no. 6 suppl., November 1995 (1995-11), pages 113S-121S, XP000907494 New York, NY, USA page 113S, right-hand column, line 20 - line 35	18,19
	-/--	

INTERNATIONAL SEARCH REPORT

Int. J. Application No
PCT/US 99/23485

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	H. WATANABE ET AL.: "Amelioration of renal disease in lupus mice genetically deficient in complement factor B." ARTHRITIS & RHEUMATISM, vol. 41, no. 9 suppl., September 1998 (1998-09), page S179 XP000914560 New York, NY, USA abstract 878	18,19
P,A	WO 98 45464 A (A+ SCIENCE INVEST AB) 15 October 1998 (1998-10-15) the whole document	18,19

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 (partially) and 2-8 (completely)

Method of treating/preventing factor B-mediated immune disease in a subject by inhibiting the activity/synthesis of factor B, by administration of an antibody to factor B. Also composition comprising said antibody

2. Claims: 1 (partially) and 9-13 (completely)

Method of treating/preventing factor B-mediated immune disease in a subject by inhibiting the activity/synthesis of factor B, by administration of an antisense oligonucleotide. Also a vector comprising said oligonucleotide and a composition comprising said vector

3. Claim : 1 (partially) and 14 and 15 (both completely)

Method of treating/preventing factor B-mediated immune disease in a subject by inhibiting the activity/synthesis of factor B, comprising administering a peptide that mimics the binding properties of factor B. Also a composition comprising said peptide.

4. Claims: 16, 17 and 20

Methods of diagnosis/prognosis of factor B-mediated disease and the effect of its treatment by determination of factor B.

5. Claim : 18 and 19

Transgenic mouse comprising a mutation in the Fas and factor B genes

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/23485

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9845464 A	15-10-1998	AU 7090298 A	30-10-1998